

Review

Review of Veterinary Acupuncture Clinical Trials

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ABSTRACT

Acupuncture has been used to treat diseases in animals for thousands of years. For the past several decades, as the use of acupuncture has increased in countries where modern Western medicine is the foundation of health care, there has been increasing scientific effort to evaluate this ancient medical treatment for objective evidence of efficacy. Clinical trials with controlled clinical conditions using either a controlled randomized or non-randomized group approach with statistical significance established for a treatment has increased among veterinary researchers. This review presents recent clinical trials involving the use of acupuncture in animals. The studies which are organized into broad categories of pain control, neurologic disease, gastrointestinal disease, disorders of sense organs and emergency medicine demonstrate its effectiveness in treating a wide range of medical conditions such as canine hip dysplasia, pain from osteoarthritis and surgery, intervertebral disc disease, seizure disorders, vomiting, inflammatory bowel disease, cardiac and respiratory depression and anxiety.

Key words: veterinary acupuncture, traditional Chinese veterinary medicine, veterinary clinical trials

Acupuncture (AP) has been used to treat a wide range of diseases in animals for thousands of years.¹ For the past several decades, as the use of acupuncture has increased in countries where modern Western medicine is the foundation of health care, there has been increasing scientific effort to evaluate this ancient medical treatment for objective evidence of efficacy.²⁻¹⁷ Clinical trials with controlled clinical conditions using either a controlled randomized or non-randomized group approach with statistical significance established for a treatment has increased among veterinary researchers.^{2,13-17} The establishment of a control group has been a challenge for these studies with several approaches tried such as sham acupuncture, use of conventional therapy or non-treated animals as controls. Thus, selection criteria for papers included in this review are: 1) randomized controlled trials (mostly with sham AP or conventional therapy as controls) with adequate numbers of patients, 2) non-randomized clinical trials (mostly group comparisons) with adequate numbers of patients under similar conditions, and 3) more limited studies which shed light on therapeutic mechanisms at work in the clinical trials are included to augment the scientific evidence that is building to support the efficacy of this treatment modality. The clinical trials presented in this review represent work from a large number of countries and substantiates the worldwide interest in

acupuncture and the continued movement to establish it as an effective evidence based medicine therapy.

PAIN

Musculoskeletal Pain in Horses

The efficacy of various frequencies of electroacupuncture for pain relief in 22 horses was systematically reviewed in a clinical trial.¹³ Focused radiant light/heat was used as a noxious stimulus and was directed onto the equine pastern to elicit the classic flexion-withdrawal reflex. Hoof withdrawal reflex latency (HWRL) was defined as the time (in seconds) between lamp illumination and the withdrawal of the hoof.¹⁸ The HWRL has proved to be a valid measurement to assess pain perception and document pain relief from acupuncture.¹³ The results suggest that electro-acupuncture (EA) treatments at high frequencies (120 Hz) induce a stronger analgesic effect than EA treatments at low frequencies (20 Hz) in local regions; however, EA treatments at lower frequencies induced longer analgesia.¹³

In another study, a double 3x3 Latin square design was applied for studying experimental lameness in 6 horses. Lameness was produced in each subject by tightening a setscrew against the sole of the hoof. Lameness grading scores of 0, 1, 2, and 3 were used to evaluate the severity of lameness. Three types of stride length were measured: total stride length (TSL), front half stride length (FHSL) and back half stride length (BHSL). The

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difference between FHSL and BHSL was defined as DFB (difference front/back). The DFB increased significantly when the horse was lame, suggesting that the DFB could be used as an objective parameter to measure lameness in horses. EA reduced the lameness score significantly in this study.¹⁴ Plasma concentrations of β -endorphin, ACTH and cortisol were measured in both of the above experiments. In addition to EA significantly increasing HWRL and reducing the lameness score, it simultaneously increased the plasma β -endorphin concentration. These results indicate that the release of β -endorphin may be the pathway in which acupuncture relieves experimental pain. None of the acupuncture treatments altered the ACTH concentrations, which indicates that ACTH is not involved in EA analgesia.¹³

Thoracolumbar pain score (TPS) is a consistent and solid pain evaluation system that is useful in evaluating the efficacy of various analgesic strategies for equine thoracolumbar pain. A prospective study was conducted to evaluate the use of electro-acupuncture in the treatment of horses with signs of chronic thoracolumbar pain.¹⁵ Fifteen horses were randomly allocated to 1 of 3 treatment groups. Horses in group 1 received electro-acupuncture stimulation (once every 3 days for 5 treatments), those in group 2 received phenylbutazone (2.2 mg/kg [1 mg/lb], PO, q 12 h, for 15 days), and those in group 3 received 0.9% NaCl saline solution (20 mL, PO, q 12 h for 15 days). Thoracolumbar pain scores were evaluated before (baseline) and after each treatment. Thoracolumbar pain scores (TPS) in horses receiving phenylbutazone and saline solution did not change significantly during the study ($P=0.999$ and $P=0.535$ respectively). After the third treatment, TPS in horses receiving electroacupuncture stimulation were significantly lower than baseline thoracolumbar pain scores ($P<0.01$) and decreased from 6.0 ± 0.6 to 2.1 ± 0.6 . These statistically significant lower scores were maintained through follow-up 14 days after the 5th treatment. Results provided evidence that three sessions of EA treatment can successfully relieve signs of thoracolumbar pain in horses and the analgesic effect induced by EA can last for at least 20 days. Alternatively the oral administration of phenylbutazone was not found to effectively relieve signs of thoracolumbar pain.¹⁵

Another clinical trial found that EA relieved chronic back pain in performance horses.¹⁶ This study was a randomized, double blind, controlled trial to evaluate electroacupuncture (EA) as a treatment for back pain in sport horses. Objective measurements of pain threshold levels were obtained with a pressure algometer. Twenty three horses with chronic back pain were divided into control (N=7) and treatment (N=16) groups. Trigger (painful) points were identified on each horse and baseline pain threshold measurements were taken. The control group received sham EA treatments with no needle penetration or electrical stimulation. Routine EA was performed in the treatment group using filiform acupuncture needles

inserted into GV-20, GV-6 and bilaterally at BL-26, BL-54, BL-21 and BL-17. Needles were connected to 5 pairs of electrical wires and an electrical impulse (4.5 volts) was delivered at a frequency of 20 Hz for 15 minutes and 80-120 Hz for 15 minutes. Both sham and control EA treatments were given over the course of 5 sessions, each spaced 3 days apart and all horses were rested during the study period. After 5 treatments, pressure induced pain was statistically significantly reduced at the trigger points in the treatment group when compared to the control group using an unpaired t-test ($p=0.034$). The conclusion was that EA and rest is an effective treatment for sport horses with chronic back pain and is better than sham EA and rest over a 15 day period.¹⁶

Rectal Pain in Horses

A clinical trial was conducted to compare the effects of electroacupuncture and butorphanol on hemodynamic and respiratory variables and rectal analgesia in mares (N=8) after controlled rectal distention. Each horse received all three of the treatments, saline (0.9% NaCl) solution (0.01 mL/kg, IV; control treatment), butorphanol tartrate (0.1 mg/kg, IV), or 2 hours of electroacupuncture (EA) at acupoints Bladder 21, 25, 27, *Bai-hui* and Stomach 36. Order of treatments in each mare was randomized. At least 7 days elapsed between treatments. A balloon was inserted in the rectum of each mare, and controlled distention of the balloon (pressures of $<$ or $=$ 220 mm Hg) was used to measure nociceptive rectal pain threshold. Both butorphanol and electroacupuncture provided statistically equal analgesia to induced rectal pain (mean \pm SD, 214 \pm 24 vs 174 \pm 35 mm Hg of balloon pressure, respectively). The conclusions and clinical relevance were that electroacupuncture and butorphanol (0.1 mg/kg, IV) may provide useful rectal analgesia in horses and electroacupuncture produces less effect on hemodynamic and respiratory variables when compared to butorphanol.^{17, 18}

Canine Hip Dysplasia

Hip Dysplasia is a common diagnosis in dogs. Multiple clinical trials have indicated that acupuncture was of benefit for pain relief in dogs with hip dysplasia.¹⁹⁻²² The most commonly used acupuncture procedures for the treatment of hip dysplasia include aqua-acupuncture (acupoint injection) and gold bead or wire implantation.²³ In a clinical study, the autologous stromal vascular fraction (SVF, n=4) or allogeneic cultured adipose-derived stem cells (ASCs, n=5) were injected into three acupuncture points (BL-54, GB-29 and GB-30) near the affected joint of dogs that were diagnosed with hip dysplasia and had previous poor response to drug therapy. After the first week of treatment, clinical evaluation showed marked improvement compared with baseline results in all patients treated with autologous SVF and 3 of 5 dogs treated with allogeneic ASCs. On days 15 and 30, all dogs showed improvement in range of motion, lameness at trot and

pain on manipulation of the coxofemoral joints, with the exception of 1 ASC-treated patient. Positive results were more clearly seen in the SVF-treated group. These results show that autologous SVF or allogeneic ASCs can be safely used for acupoint injection in the treatment of hip dysplasia in dogs and represent an important therapeutic alternative for this type of pathology.¹⁹

In another study, seventy-eight dogs with pain due to hip dysplasia were studied in a controlled, double-blinded clinical trial to evaluate gold bead implantation as a pain-relieving treatment. The dogs were randomly assigned to two groups; 36 in the gold implantation group and 42 in the placebo group. Both groups were treated equally regarding anesthesia, hair clipping and penetration of the skin with the same type of needle. The gold implantation group had small pieces of 24 carat gold inserted through needles at five different acupuncture points and the placebo group had the skin penetrated at five non-acupuncture points (sham points) so as to avoid any possible effect of stimulating the acupuncture points. There was statistically significant greater improvement in mobility and greater reduction in the signs of pain in the dogs treated with gold implantation than in the placebo group.²⁰ There was good correlation between veterinary and owner assessments as well.²⁰

It is very interesting to note that the same group published a similar study one year earlier and indicated age and placebo effect might affect the outcome.²¹ In this study, eighty dogs diagnosed with hip dysplasia were allocated to gold bead implantation (n=38) and placebo (n=42). After six months, 33 of the 42 placebo-treated dogs received gold bead implantation in an open study lasting a further 18 months. The blinding procedure used in the study (owners unaware of treatment group) resulted in 60% of the owners correctly guessing the treatment given. Of those who guessed the treatment erroneously, 88% believed the treatment given was gold bead implantation; thus suggesting a placebo effect.²¹ The researchers then conducted a two-year follow-up double blinded study on dogs with pain from hip dysplasia used in the trial with only the owner blinded and found 30 of the 36 dogs (83%) in the gold implantation group showed significant improvement ($p = 0.02$), which included improved mobility and reduction in the signs of pain, compared to the placebo group (60% improvement).²²

Two extensive review papers (Part 1: Background and current state of research, Part 2: Clinical trials and case reports) from German research summarized important findings about the effects of gold implanted in tissue for the treatment of canine hip dysplasia.²⁴⁻²⁵ After providing an overview of the historical use of gold and gold compounds, the technique of implanting the metal is introduced and publications concerning the effects of gold implantation in tissue are presented and summarized. Additional study comparing anti-inflammatory effects of gold implantation to treatment with non-steroidal anti-

inflammatory drugs is recommended.

Although not clinical trials, case reports from Brazil and Italy using gold bead implants at acupuncture points successfully in single clinical cases add to the body of literature which supports the benefit of acupuncture for hip dysplasia in dogs.^{26, 27}

Post-surgical Pain

Another study examined the effect of acupuncture on post-surgical pain after an abdominal procedure.²⁸ Zoletil (Tiletamine) is a common veterinary anesthetic agent. Twenty-five dogs were randomly divided into 5 groups: normal-dose zoletil (6 mg/kg), acupuncture + 1/3-dose zoletil, acupuncture + 1/2-dose zoletil, acupuncture + 2/3-dose zoletil and untreated control (no acupuncture, no zoletil). The first four groups received surgery with an abdominal incision after anesthesia. Plasma samples of 7 time points were collected for detection of catecholamine (CA) and opioid peptide (OP) by enzyme linked sorbent (ELISA) in the experimental groups and compared with the blank group. Plasma concentration of OP in acupuncture + 1/3 zoletil group was significantly higher than normal-dosage zoletil and blank control groups. The plasma concentration of CA was found to decrease with a rise in the OP. In contrast, the plasma concentration of CA in the normal dosage group did not change after anesthesia. In the blank group, the plasma concentration of CA decreased after recovering from anesthesia while the OP concentration had no obvious change. This study demonstrated that acupuncture could decrease the dosage of anesthetic required for abdominal surgery. Acupuncture also increased the level of endogenous opioid peptide and this was attributed to the effect of regulating catecholamines.²⁸

Several studies have found that acupuncture can provide sufficient analgesia for surgical procedures in cattle, cats and dogs.²⁸⁻³² A controlled study using 28 animals found that a level of surgical analgesia graded as 'excellent' was produced in 87.5% of cattle treated with EA alone at dorsal acupuncture points.²⁹ Consciousness was maintained and the cattle remained standing, with pain sensation lost in an area appropriate for an abdominal surgical approach. Pain was still present in all cattle in the control group, which received EA at non-acupuncture points. This replicates the findings of an earlier study, which compared EA-induced analgesia to that produced by a paramedian nerve block suitable for laparotomy.³⁰

Another study examined the effectiveness of using acupuncture to relieve pain after ovariohysterectomy (OVH) surgery.³¹ Twenty-nine healthy cats, aged 11.59 ± 6.21 years and weighing 2.50 ± 0.58 kg were used and assigned to four groups: aqua-acupuncture (GA; n=7, 0.1mL of saline solution in the SP-6, GB-34, LIV-3 and ST-36 acupoints bilaterally), meloxicam (GM; n=8, 0.1mg/kg of meloxicam SQ), pharmacopuncture (GMFV; n=7, 0.01

mg/ kg of meloxicam, diluted to 0.8ml of saline solution, equally distributed in the SP-6, GB-34, LIV-3 and ST-36 acupoints bilaterally) or a reduced dose of meloxicam (GMFF; n=7, 0.01mg/kg of meloxicam diluted in saline SQ in the interscapular region). The animals underwent OVH by a minimally invasive surgical technique. A blind assessor at 1h, 2h, 6h, 8h, 12h and 24h evaluated the patients after surgery, using a visual analog scale (VAS) and a descriptive pain scale (DPS). An analgesic rescue was performed with 0.2mg/kg of morphine IM when the DPS score increased more than 33% from baseline. Four analgesic rescues were performed in GM group, three in GA and GMFF groups and two in GMFV group. There was no statistical difference between groups for the physiological variables, VAS for pain and sedation and DPS. All treatments showed similar analgesic effect in cats undergoing OVH.

The effectiveness of electroacupuncture for pain control in cats undergoing ovariohysterectomy was studied as well. Eighteen healthy cats were equally distributed in three groups: Electroacupuncture, morphine and sham-control. Animals were anesthetized with acepromazine, propofol and isoflurane. Needles were introduced in sham-acupoints on animals in both the sham-control and morphine groups and in acupoints ST-36 and GB-34 in electroacupuncture group animals. Electroacupuncture was performed with 2 and 100Hz using a square wave. Animals from the morphine group received morphine (0.3mg/kg IM) and control animals received no treatment. Data were recorded just before acepromazine administration, 10 minutes after acepromazine administration, after anesthetic induction and stabilization, 30 minutes after treatment with either electroacupuncture or morphine injection, and then every 10 minutes for 60 minutes. Variables recorded were rectal temperature, respiratory frequency, heart rate, oxyhemoglobin partial saturation, mean arterial pressure and inspired isoflurane volume. Only the animals receiving electroacupuncture did not show a significant difference between measurements for mean arterial pressure, while electroacupuncture and morphine groups had better cardiac stability. Compared to the control group, the inspired isoflurane volume was decreased by 58.33% in the electroacupuncture group and 22.01% in the morphine group. It was concluded that electrostimulation of ST-36 and GB-34 in cats undergoing elective ovariohysterectomy results in a decreased inspired isoflurane volume, leading to improved cardiorespiratory stability when electroacupuncture is compared to morphine.³²

NEUROLOGIC DISEASES

Intervertebral disc disease (IVDD) in Dogs and Cats

In one study, fifty dogs with thoracolumbar IVDD were classified using a scale of specific neurological deficits from Grades 1-5 (Grade 1 = pain only, no

neurological deficits and Grade 5 = paraplegia with no deep pain) and then randomly allocated to one of two treatment groups.¹⁰ Dogs in one group received electroacupuncture (EA) combined with standard conventional medical treatment and those in the second group received only standard conventional medical treatment. The time (mean \pm standard deviation) to recover ambulation in dogs with Grade 3 or 4 dysfunction (non-ambulatory) in the group receiving EA was significantly less (10.10 ± 6.49 days) than in the group not receiving EA (20.83 ± 11.99 days). The success rate, defined as the ability to walk without assistance for dogs with Grade 3 or Grade 4 dysfunction (non-ambulatory), was significantly higher (10/10 dogs) in the group that received EA than similarly affected dogs not receiving EA (6/9 dogs). The overall success rate (all dysfunction grades) for dogs receiving EA was significantly higher (23/26; 88.5%) than for those receiving only conventional medication (14/24; 58.3%). The conclusion of the study was that EA combined with standard conventional medical treatment was more effective than conventional medication alone and resulted in a shorter time to recover ambulation in dogs with thoracolumbar IVDD.³³

In another study comparing surgery and EA for dogs with IVDD, 40 dogs, whose neurological deficits were graded using the same Grade 1-5 scale described above, were divided into three treatment groups: 1) Prednisone and decompressive spinal surgery alone (10 dogs), 2) Prednisone and EA alone (19 dogs) and 3) Prednisone, decompressive spinal surgery and EA (11 dogs).³⁴ Treatment was considered a "clinical success" when a dog initially classified as Grade 4 or 5 (paraplegic with or without deep pain respectively) became a Grade 1 (no neurological deficits) or Grade 2 (ambulatory) within six months of initiating treatment. The researchers found that "clinical success" was significantly higher for dogs that received EA alone (15/19) or EA and surgery (8/11) than for dogs that had surgery alone (4/10). Thus, they concluded that EA was more effective than surgery alone for recovery of ambulation and improvement in neurologic deficits in dogs with long-standing severe deficits attributable to thoracolumbar IVDD.³⁴

The outcomes of eighty dogs with paraplegia and intact deep pain from intervertebral disk disease treated with or without EA were compared in a retrospective study.¹² Thirty-seven dogs were treated with prednisone alone and forty-three dogs were treated with prednisone plus EA. The combination of EA with prednisone was more effective than prednisone treatment alone to recover ambulation, relieve back pain and decrease relapse.³⁵

Fifteen dogs undergoing surgery because of acute thoracolumbar disk disease were alternately assigned to treatment (conventional analgesics and adjunct EA) and control (conventional analgesics alone) groups. For dogs in the treatment group, acupuncture was performed as

soon as the dog was awake after surgery and then every 12 hours until the end of the study period (72 hours after surgery) was reached. Total dose of fentanyl administered during the first 12 hours after surgery was significantly lower in the treatment group than in the control group even though dosages of analgesics administered from 12 through 72 hours after surgery did not differ between groups. Pain score was significantly lower in the treatment group than in the control group 36 hours after surgery, even though it did not differ significantly between groups at any other time.³⁶

Acupuncture has been used for the treatment of IVDD in cats as well. A 14-year-old male neutered domestic shorthair cat with multifocal intervertebral disc disease (IVDD) characterized by dorsal disc protrusion throughout the thoracic and cranial lumbar spine was treated with several modes of acupuncture treatment including dry needle acupuncture, EA and scalp acupuncture along with *Tui-Na* and physical therapy. Significant improvements in mobility, proprioception and spinal posture were noticed and the cat was able to rise, walk and run 4 months after acupuncture treatment initiation.³⁷

IVDD Mechanistic Studies

Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) is a common method for detecting DNA fragmentation that results from apoptotic signaling cascades. EA treatment decreased the number of TUNEL-positive apoptotic cells in lamina II of the L(3) and L(6) cord segments at 7 and 14 days post operation (DPD). This EA-mediated neuroprotection was associated with a decrease in the number of Bax immunoreactive neurons and an increase in the number of Bcl-2 immunoreactive neurons. Furthermore, Western blot and RT-PCR analysis revealed a significant downregulation of Bax protein and its mRNA, but an upregulation of Bcl-2 in the dorsal horn of L(3) and L(6) cords at both 7 and 14 DPD. The study findings suggested that EA could inhibit neuronal apoptosis in the dorsal root of a spinal cord, possibly by Bax downregulation and Bcl-2 upregulation in cats that had received partial dorsal root ganglionectomy.³⁸

Ciliary neurotrophic factor (CNTF) plays a crucial role in neurite outgrowth and neuronal survival both in vivo and in vitro. Another study was designed to investigate the effects of EA on CNTF expression in the spared L(6) dorsal root ganglion (DRG), and spinal lamina II at spinal segments L(3) and L(6) as well as nucleus dorsalis (ND) of L(3) spinal segment following removal of L(1)-L(5) and L(7)-S(2) (DRG) in cats. After EA treatments, immunoreactive neurons in L(6) DRG noticeably increased at 7 DPD, compared with the non-acupunctured group. CNTF immunopositive neurons in the ND of L(3) segment returned to the sham-operated level at 14 DPD. After EA, their number significantly increased as early as 7 DPD in lamina II of L(6) segment,

and as late as 14 DPD in ND of L(3) segment. This study concluded that CNTF expression was involved in the EA promoted plastic changes in L(6) DRG and the associated deafferented spinal lamina and ND.³⁹

Seizure Disorders in Dogs

A study of 15 dogs with uncontrolled idiopathic epileptic seizures was evaluated both clinically and with electroencephalographic (EEG) recordings under anesthesia to assess the effect of gold implantation acupuncture. A first EEG recording was performed before the treatment protocol and a second EEG was performed 15 weeks later. The acupuncture treatment protocol was carried out by implanting 2–3 mm gold wire pieces into the following acupuncture points: GB-20, GV-23, GV-21, GV-20, GV-16, GV-14, auricular *Shen-men*, *Yin-tang*, LI-4, LIV-3, ST-40. Implants were placed subcutaneously or intramuscularly (depending on the point) using a 20 gauge needle and a plunger. There was a significant mean difference ($P < 0.05$) in seizure frequency and seizure severity at 15 weeks with 9 of the 15 dogs (60%) demonstrating at least a 50% reduction in seizure frequency.⁴⁰

Ear acupuncture was used for 11 uncontrolled epilepsy dogs with the mean age of 5.8 years and the mean bodyweight of 26 kg. Ear acupuncture needles were implanted in the auricular acupoint *Shen-men* in both ears. The needles were left in place for a duration of 4 days to 4 months (mean 2 weeks). The needles were replaced (mean four times) on a 3-9 week basis. After this auricular acupuncture treatment, 4 dogs were seizure-free, 3 had decreased frequency of seizures, and 4 showed no amelioration. Of the 7 dogs that received anti-epileptic drugs before acupuncture treatment, 1 was seizure-free and completely weaned-off medication, 1 was kept on half-dose medication with marked improvement, 3 were maintained on lower drug doses (-33/-50%) with no clinical deterioration, 2 dogs with continued seizures were reported to have shorter or absent prodromal and postictal periods.⁴¹

Five epileptic dogs, which were nonresponsive to high levels of anticonvulsants, were presented to the acupuncture clinic at the Veterinary Hospital of the University of Pennsylvania for treatment. Acupuncture was performed by placing small gold implants subcutaneously over the calvaria at acupuncture points on the Governing Vessel (GV), Gall Bladder (GB), and Bladder (BL) meridians and left in place to provide constant stimulation to the points. Each of the five dogs treated showed a change in seizure patterns following gold implant placement. Two dogs had decreases in seizure frequency with no change in their medication, but they reverted to their previous pattern approximately five months after treatment. Three dogs continued to have decreased numbers of seizures and were maintained on decreased levels of anticonvulsants.⁴² Similar results were found in auricular acupuncture

treatment of epilepsy in 5 dogs that were presented to Veterinary Medical Teaching Hospital of the University of Florida.⁴³ Although these studies were on a small scale, it is promising evidence for acupuncture's effects on normalizing neurological function in epileptic animals, and merits further scientific investigation.

Seizure Mechanistic Studies

The effect of acupuncture on epilepsy along with its mode of actions have both been studied in lab animals.⁴⁴⁻⁴⁵ Adult male Sprague Dawley rats with a body weight of 180–220 g were randomly grouped into untreated control (n = 4) and experimental-induced epilepsy (n = 63) groups. Furthermore, the epileptic animals were randomly subdivided to a group of epilepsy only (n = 10) and epilepsy plus EA groups (n = 53). EA with a low-frequency (10 Hz/1 mA) or high-frequency (100 Hz/1 mA) current was applied to the epileptic rats for 30 minutes. Four pairs of acupoints were tested, *Shui-gou* (GV-26) + *Da-zhui* (GV-14), *Jin-suo* (GV-8) + *Yao-qi*, *Nei-guan* (PC-6) + *Qu-chi* (LI-11), and *Feng-long* (ST-40) + *Yong-quan* (KID-1). The results demonstrated that: 1) low- or high-frequency EA at different acupoints reduced epileptic seizures ($P < 0.05$ versus the control) with an exception of low-frequency EA at PC-6 and LI-11; 2) low-frequency EA induced a better effect at ST-40 plus KID-1 than that of the other acupoints ($P < 0.05$); 3) there is no significant difference in the effects of high-frequency EA at these acupoints; 4) the high-frequency EA elicited a greater effect than that of low-frequency EA in all groups ($P < 0.05$), with an exception at GV-8 + *Yao-qi*. The researchers conclude that EA attenuation of epileptic seizures is dependent on the stimulation parameters and acupoints and that the delay in appearance of the EA effect could be a reflection of the time required by the EA signal to regulate neural function in the central nervous system.⁴⁴ In an additional study, electrical stimulation of ear points may reduce seizures by suppressing the release of somatostatin and excitatory amino acid neurotransmitters (i.e., aspartic acid and glutamine) and by promoting inhibitory amino acid neurotransmitter release (i.e., glycine, taurine, and GABA).⁴⁵

Laryngeal Hemiplegia in Horses

Eighteen thoroughbred horses (11 males and 7 females, aged from 1 to 4 years) with laryngeal hemiplegia (grade IIa to IIb) received electro-acupuncture, once a week for a total of three to seven sessions, depending on the severity of the hemiplegia. The electro-acupuncture treatment was used at 20 Hz for 10 minutes, then at 80 to 120 Hz for 10 minutes at 7 pairs of acupoints: left CV-23 and GB-21, left LI-18 and LI-17, bilateral *Hou-shu*, left ST-9 and *Hou-bi*, left SI-17 and LI-15, right ST-9 and *Hou-bi*, right SI-17 and LI-15. The electrical intensity was increased several times to maintain minimal muscle contraction during the treatment sessions. All the horses

were examined endoscopically by the same single-blind observer (equine practitioner) initially and 1-2 days after the last electro-acupuncture treatment. The endoscopic grades of hemiplegia had improved in all 18 horses: 13 returning to normal while 6 improved at least one grade. The respiratory noise during training was also clinically significantly improved after the treatment.¹²

INTERNAL MEDICINE

Gastrointestinal Disorders in Dogs and Cats

A double-blinded clinical study containing 222 dogs divided into 6 treatment groups evaluated the incidence of retching, vomiting and signs of nausea secondary to morphine administration. Treatments included maropitant (Cerenia), acepromazine, electroacupuncture at 1 or 5 points, sham acupuncture, and a saline control group. The incidence of vomiting and retching events in the maropitant (21), 5-acupoint (34), 1-acupoint (35), and acepromazine (38) groups was significantly lower than in the saline control (88) and sham-acupoint electroacupuncture (109) groups. Mean nausea scores for the saline control group, maropitant, and sham-acupoint electroacupuncture groups increased significantly after morphine administration, whereas those for the acepromazine along with the 1 and 5 acupoint electroacupuncture groups did not. Study conclusion indicated that maropitant treatment had the lowest incidence of vomiting and retching, however, acepromazine and electroacupuncture appeared to prevent an increase in severity of nausea following morphine administration to dogs.²

A study was conducted to evaluate the anti-emetic effect of oculo-acupuncture and to compare the results to the anti-emetic effect of body acupuncture. Twelve dogs induced to vomit by xylazine were selected with a Latin Square design and had a 1 week wash out interval between treatments. The study dogs were placed into 4 groups (3 acupuncture treatment groups with acupoints located in different regions and one control group). The vomiting rates of acupuncture group 1 (50%, $p < 0.05$), acupuncture group 2 (58.3%) and acupuncture group 3 (41.6%, $p < 0.01$) were lower than that of the control (100%) group. This study demonstrated that acupuncture had anti-emetic effects on dogs with xylazine-induced vomiting.⁴⁶

In another study the effect of acupuncture on canines with inflammatory bowel disease was studied. Eighteen canines with body weights of 3-3.5 kg and experiencing weight loss and anorexia were randomly divided into 3 groups: control (A), GI Disorders without treatment (B) and GI disorders with acupuncture treatment (C). Study dogs in groups B and C were injected with 0.15 mg/kg reserpine subcutaneously once a day (exacerbate GI adverse effects), while dogs in group A were injected with normal saline. The acupoints ST-36 and BL-20 of group C dogs were treated with dry needling technique 20 minutes

once daily for 7 days. Results showed that the body weights of the study dogs in Group B were lower than Group C ($P<0.05$). After 7-days of acupuncture treatment, the levels of pepsin, trypsin and motilin in Group C were upregulated (increased to within normal limit) ($P<0.05$) while the contents of gastrin and somatostatin in Group C were downregulated (decreased to within normal limit) ($P<0.05$) as compared to Group B. The authors concluded that acupuncture at ST-36 and BL-20 would alleviate clinical signs, promote weight gain, and regulate digestive function in dogs with GI disorders.⁵³ These studies along with an extensive systemic review of studies show that acupuncture has significant and clearly described effects on the animal gastrointestinal tract, which has great clinical relevance given the limited clinical efficacy of conventional medical treatment for disorders such as inflammatory bowel disease in dogs and cats.⁵⁴

Gastrointestinal Mechanistic Studies

Anti-emetic effects of acupuncture on vasopressin-induced emesis; gastro-duodenal motor activity and the frequency of retching and vomiting were simultaneously recorded in conscious dogs. Electroacupuncture (EA, 1-30 Hz) at PC-6, BL-21, or ST-36 was performed before, during and after the vasopressin infusion. To investigate whether the opioid pathway is involved in EA-induced antiemetic effects, naloxone (a central and peripheral opioid receptor antagonist) or naloxone methiodide (a peripheral opioid receptor antagonist) was administered before, during, and after EA and vasopressin infusion. Intravenous infusion of vasopressin induced retching and vomiting in all dogs tested and was accompanied by retrograde peristaltic contractions before the onset of retching and vomiting. EA (10 Hz) at PC-6 significantly reduced the number of episodes of retching and vomiting and suppressed retrograde peristaltic contractions. In contrast, EA at BL-21 or ST-36 had no anti-emetic effects. The anti-emetic effect of EA was abolished by pretreatment with naloxone but not naloxone methiodide. It is suggested that the anti-emetic effect of acupuncture is mediated via the central opioid pathway.⁴⁷

The acupuncture point ST36 is suggested in Traditional Chinese Medical (TCM) theory to affect the stomach. A study using Positron Emission Tomography (PET) scans has shown that when ST36 is stimulated with an acupuncture needle, there is increased activity in the regions of the human brain associated with gastric function. This study provides convincing support of the TCM theory that specific acupuncture points are related to specific organs.⁴⁸ A study using an electrogastragram to monitor stomach muscle activity in rabbits demonstrated that electroacupuncture at ST36 has a bi-directional, modulatory effect on stomach muscle electrical activity, possibly through M-cholinceptors and α -adrenoceptors.⁴⁹ Other acupuncture points that have demonstrated an effect on gastrointestinal motility in animals include BL27,

BL21 and SP6.^{50, 51, 52}

EMERGENCY MEDICINE

Resuscitation

Respiratory depression or apnea during anesthesia is common in veterinary practice. A study of 69 cats and dogs demonstrated that acupuncture at the acupoint GV-26 restored respiration to normal or near normal rates within 10 to 30 seconds of needle insertion in 100% of animals if there was no concurrent cardiac arrest. When cardiac arrest occurred and vital signs were absent, the revival rate was 43 per cent.⁵⁵

On examination of 243 cases of 17 different species of domestic and exotic animals and birds, acupuncture resuscitation for anesthetic apnea has approached almost 100% efficacy in clinically healthy dogs, whereas in animals affected with different diseases the success of intervention was smaller (77.47%). In zoo animals suffering from narcosis, the resuscitation effectiveness achieved is 92.6%. The resuscitation effect is based not only on strictly determined points but also on diffusive irritation of the respective point and its surroundings by acupressure. The authors discuss the factors on which the acupuncture resuscitation and its success are dependent.⁵⁶

BEHAVIOR

Stress Response

Acupuncture has been shown to have the beneficial effect of reducing stress responses in horses.⁵⁷ A study was conducted to compare the effects of injecting the standard dose of acepromazine (ACP) (0.1 mg/kg, IM) with those of aqua-acupuncture (1/10 of the standard acepromazine dose at the acupoint GV-1) on the stress responses of healthy horses undergoing road transport for 2.5 hours. Four different treatments were applied immediately before loading, with 8 animals divided into four treatment groups. The first group received injections of saline IM at the base of the neck (CTL-SAL); the second group (CTL-ACP) received ACP (.1mg/kg IM) at the base of the neck; the third group (GV1-SAL) received an injection of saline into GV-1 acupoint; the fourth group (GV1-ACP) received ACP (.01mg/kg) at GV-1 acupoint. The road transport increased heart rate (HR), respiratory rate (RR), body temperature, and serum cortisol of the untreated horses (injected with saline at the base of the neck). Aqua-acupuncture at GV-1 (GV1-ACP) with decreased dose ACP (0.01 mg/kg) reduced the average HR and transport-induced increase in HR at unloading, without changing the other variables. The CTL-ACP treatment had significantly lower RRs than those of CTL-SAL and GV1-SAL after transport ($P < .01$) but without preventing the stress-induced increase of cortisol.⁵⁷

DERMATOLOGY AND SENSE ORGANS

Malassezia Otitis

Acupuncture has been shown to be helpful in the treatment of malassezia otitis in dogs.⁵⁸ Ten dogs with confirmed malassezia otitis were used in the study. One group was treated with ketoconazole, the second group was treated with a combination of a topical aromatherapy product and SI-19 acupoint injection twice, 24 hours apart. Both groups had a significant clinical improvement, however the ketoconazole treated group experienced significant elevations in their ALT levels. Although there was not a treatment group with acupuncture alone, this study demonstrates that acupuncture with holistic treatment of malassezia otitis shows promise without the significant liver enzyme elevations that can occur with traditional treatment.

PRODUCTION ANIMAL MEDICINE

Mastitis

Eighteen Holstein-Friesian X Sahiwal crossbred lactating cows, 3-8 years old, previously diagnosed with mastitis were used to evaluate the effect of acupuncture on mastitis and milk production.⁵⁹ The animals were distributed randomly into one control (non-treated) and two acupuncture treatment groups (conventional white needle acupuncture (CWNA) and acupuncture), with six animals per group. For the acupuncture groups, two acupoints, *Bai-Hui* and *Nyukon* were stimulated daily for three consecutive days during week 1 of the study and then again for three consecutive days during week two. The CWNA group was stimulated by thrusting and twirling of filiform needles for one minute at five minute intervals for 20-30 min daily. For the aqua-puncture group, 1 ml of 1% chilli pepper decoction was injected into each acupoint using a hypodermic needle. The observation period lasted for three months. Improved mastitis control was observed in the acupuncture groups but not in the control group. The average daily milk production presented as percentage change in milk production showed that the control group had the steepest decline while CWNA group had the least decline. The above results suggest that acupuncture has the potential to decrease incidence of mastitis while both CWNA and acupuncture have the potential to increase milk production.⁵⁹

Abomasal Displacement

A study was performed to assess the efficacy of moxibustion after rolling correction in dairy cows with abomasal displacement (AD).⁶⁰ The experimental group was comprised of 86 Holstein cows over a 2 year period with left (LDA) or right (RDA) displacement of the abomasum, with a mean age of 3.8 years. The cows were rolled for correction of AD. After the rolling procedure, moxibustion was conducted on six acupoints (BL-20, BL-21 and BL-26) once daily during the course of treatment.

During follow-up 1 week later, 67 (93.1%) of 72 LDA and 12 (85.7%) of 14 RDA cows still maintained the abomasum in the correct position and were released as cured after moxibustion. Rolling a cow through a 180° arc after casting her corrects most LDAs; however, recurrence is likely.⁶¹ This study demonstrated that moxibustion effectively treats AD by maintaining the abomasum in normal position following rolling correction in dairy cows.

Retained Placenta

A clinical study demonstrated that an aqua-acupuncture of herbals at GV-1 can prevent retained placenta in cows.⁶² One hundred and twenty four pregnant dairy cows were selected as an untreated control group and observed after calving to determine the retained placenta rate for the farm. Fifty-two pregnant dairy cows from the same farm were selected for the study and randomly assigned to two groups: 30 cows in the herbal *Dang Hong Fu* group and 22 cows in a saline control group. Immediately after calving 40 ml of *Dang Hong Fu* (40 grams of dried herbs) was injected into GV-1 in the herbal group and 40 ml of physiological saline was injected at the same site in the saline control group. Both groups were observed for retained placentas and the time until placental expulsion was recorded in the others. The retained placenta rate for untreated cows that received no treatment was 35.5% (44/124). The incidence of retained placenta in the *Dang Hong Fu* group was 16.7% and in the saline control group 31%. The time for expulsion of placental membranes was a mean of 9 hours (range 3.5-24 hours) in the *Dang Hong Fu* group and a mean of 14.7 hours (range 3.0-24 hours) in the saline control group. When compared to the untreated control group, *Dang Hong Fu* aqua-acupuncture at GV-1 significantly reduced the incidence of retained placentas ($p < 0.047$; < 0.05), but saline aqua-acupuncture did not ($p = 0.740$; > 0.05). Herbal aqua-acupuncture may offer an easy treatment method to reduce the incidence of retained placenta with no adverse side effects.

SUMMARY

The veterinary literature was reviewed for clinical trials that have been performed evaluating the efficacy of acupuncture treatment in animals, with particular emphasis on the past 10 years. An attempt was made to select studies that were randomized controlled trials (mostly with sham AP or conventional therapy as controls) with adequate numbers of patients to allow statistical evaluation or non-randomized clinical trials (mostly group comparisons) with adequate numbers of patients under similar conditions. In addition, more limited studies that provided insight on therapeutic mechanisms at work in the clinical trials were included to augment the scientific evidence that is building to support this treatment modality. The studies were organized into broad categories of pain control, neurologic disease, gastrointestinal disease, dermatology,

emergency medicine, behavior and production animal medicine.

Pain control was a large section of 12 studies that included musculoskeletal and rectal pain in horses, hip dysplasia in dogs and surgical pain in dogs, cats and cattle. The studies ranged in animal numbers from the smallest at 8 animals (rectal pain) to large studies of 80 animals looking at control of pain associated with hip dysplasia. Neurology was the second largest area with 8 studies evaluating either IVDD or seizures. Animal numbers were large in the IVDD studies ranging from 50 to 80 while seizure studies were smaller with 5 to 15 animals. Both gastrointestinal (GI) and production animal medicine had smaller numbers of studies at 3 each but large numbers of animals in these clinical trials (GI: 12 to 222 animals, production animal: 18 to 124). Emergency medicine had 2 clinical trials looking at resuscitation with 1 large trial containing 17 different species and 243 subjects. Behavior and dermatology had 1 study each with 32 and 10 animals respectively.

The results of these clinical trials with acupuncture, under the scrutiny of evidence-based clinical applications, demonstrated efficacy in a wide range of diseases. There was improved pain control in horses for a variety of issues including hoof, chronic back soreness, thoracolumbar and rectal pain. Electro-acupuncture with high frequencies appeared to be more effective than using lower frequencies. In addition, acupuncture methods with surgery were evaluated with successful decreases in anesthesia as well as improved pain control. Clinical trials demonstrated the effectiveness of using acupuncture to treat dogs with hip dysplasia. Techniques most often used included either acupoint injection or gold wire or bead implantation at the acupoint sites. In addition to reducing pain, a clinical trial evaluating indicators of stress in horses demonstrated reduction of these parameters with acupuncture.

In neurology, acupuncture was shown to be effective in the treatment of intervertebral disc disease (IVDD) in both dogs and cats. Electro-acupuncture combined with traditional medical treatment was more effective than medical treatment alone. A separate study found that dogs that required surgery for thoracolumbar IVDD did better postoperatively if the surgery was combined with electro-acupuncture. In addition, gold bead or wire implantation, traditional needle acupuncture and ear acupuncture proved effective in the treatment of seizures. These techniques were shown to reduce the frequency and severity of seizure activity as well as potentially allowing successful management of the seizure patient on lower doses of anti-convulsants.

Acupuncture can be used in the treatment and prevention of vomiting in dogs, most likely because of mediation of the central opioid pathway. The acupuncture points PC-6, ST-36, BL-20, BL-21 and SP-6 appear to be effective in the treatment of vomiting in dogs. Inflammatory bowel disease responded to acupuncture

treatment at ST-36 and BL-20 as well. Resuscitation as demonstrated in 2 large studies is assisted by needling the acupoint GV-26 and should be considered in the treatment of respiratory depression, apnea or cardiac arrest. Clinical trials performed in cattle demonstrated cost effective and efficacious use of acupuncture in the common production diseases of mastitis, abomasal displacement and retained placenta.

Although the strength of the clinical trials cited in this review vary, acupuncture demonstrated safety and efficacy in the treatment of a number of conditions in animals. Future well-designed studies are needed in order to strengthen the recommendation for acupuncture in the treatment of animal disease from an evidence-based medicine perspective and it is hoped that research groups will continue to increase the numbers of these studies.

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ABSTRACT

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TCVM diagnosis and treatment approach to equine juvenile physitis

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Physitis, also known as epiphysitis or physeal dysplasia, is a generalized bone disease of young, growing horses that is characterized by the enlargement of the growth plates in long bones such as the tibia, radius, and cannon bones. The disease is most common in foals four to eight months of age undergoing rapid growth, but can be seen in maturing horses up to two years old. While the exact cause of this condition is unknown, rapidly growing young horses that are fed high calorie diets are at highest risk. Uncomplicated physitis (non-septic or non-fractured) is typically considered self-limiting and managed with diet modification, exercise restriction, and non-steroidal anti-inflammatories. Objective evidence and peer-reviewed publications on this condition are rare at best. Understanding a TCVM approach to physitis may benefit these patients and speed healing through the use of acupuncture, food therapy, herbal support, and constitutional balancing. The TCVM pathways of physitis, and two case examples are presented.

***Jing* Deficiency and Physitis**

A *Jing* deficiency results in a *Wei Qi* deficiency that allows the External Pathogenic Factors (EPF) to penetrate to the *Wei* and *Jing* levels. The joints are where the body's defenses are concentrated and the pathogenic factors are sequestered. *Bi* syndrome includes all three EPF: Wind, Damp, and Cold. The syndrome is named for the EPF that dominates.

Case 1: Yearling APHA gelding presented for a second opinion on acute knuckling and inability to stand. Joints were grossly swollen and warm. Patient has an Earth constitution and was being fed excessive amounts of grain and supplements. Osseous changes were visible on radiographs. Kidney *Jing* Deficiency, Spleen *Qi* Deficiency and Damp physitis was diagnosed. This case highlights the phenotype, nutritional and lifestyle stresses that are pathogenic for physitis.

Case 2: A four-month-old APHA filly, being prepared for showing as a weanling was presented for swollen, knuckling fetlock joints with osseous changes on radiographs. She was being fed high calorie foods and dewormed excessively (4 doses ivermectin in 2 months) prior to being sold to her current owner. Although the joints had cooled, the patient still had swollen joints and knuckling at presentation. *Jing* Deficiency, Liver and Spleen Damp Heat and Stagnation was diagnosed. This case highlights changes in a Wood constitution filly secondary to stress (Liver injury), along with phenotypic and nutritional stress resulting in physitis.